New advances in MDR treatment. Polymyxin and Nephroprotective agents.

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NOIGEL LLC is a New York based company and established in 2010.

Our mission is to find new innovative ways to treat MDR infections.

Amongst the company’s expertise is utilizing synergistic combinations of FDA approved generic drugs and developing pharmaceutical compositions with new and unique applications.

NOIGEL scientists have published extensive research studies supporting development of their pharmaceutical compositions.
CDC Statistics gram neg MDR threat

https://www.cdc.gov/drugresistance/biggest_threats.html
Current research strategies within scientific community.

MDR gram-neg bacteria

- Engineered bacteriophages
- Immune stimulation
- Antimicrobial peptides
- Antibodies
- Probiotics
- Vaccines
- Pharmaceuticals on Improving compounds
- NIH, NIAID Antibiofilm peptides
- Antibiotic potentiaters
- Antibiotic adjuvants

http://jb.asm.org/content/198/19/2572.full
The cost of antibiotic resistance to U.S. health care system

- A 2011 IDSA (Infectious Diseases Society of America) survey found more than 60 percent of surveyed infectious-disease specialists had seen a pan-resistant, untreatable bacterial infection within the prior year.
- HAIS (Healthcare-Associated Infections) cause 99,000 deaths in the nation every year. Antibacterial-resistant pathogens cause most of these deaths.
- Sepsis and pneumonia caused nearly 50,000 U.S. deaths in 2006. These two HAI s cost the U.S. healthcare system more than $8 million in 2006.
- Antibiotic-resistant infections lengthen patients' hospital days by an average of 6.4 days to 12.7 days.
- Antibiotic-resistant infections cost the U.S. economy nearly $20 billion in healthcare costs and $35 billion each year lost productivity.
Market Opportunity

12
Only 12 New antibiotics FDA approved in last 5 years *

4-9%
Annual Increase in global anti-MDR bacteria antibiotic market*

$246 Mill. USD
Amount to spend in Pharma and academia to fight MDR bacteria**

* https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm595264.htm
Polymyxin and Nephrotoxicity

• Polymyxin B was first patented in 1952.

• Polymyxin nephrotoxicity has made it a less desirable treatment over the years.

• As per NIH report Polymyxin B has resurged in recent years as a last resort therapy for Gram-negative MDR and extremely drug resistant (XDR) infections.

NOIGEL has developed pharmaceutical compositions that decrease Polymyxin’s nephrotoxicity and increase efficiency to fight MDR bacteria.
Past strategies on Polymyxin Nephrotoxicity

• Polymyxin IV administration in different doses and different time ranges.¹

• Analyzing drug delivery methods (e.g.s IV, IM or SQ).²

• Diverse methods of Polymyxin production and purification.³

NOIGEL’S Research Project

Research Base:
NOIGEL LLC: Laboratory of Immunopharmacology
Laboratory of Biochemistry and Biotechnology

Testing Method
NOIGEL performed in vivo testing of Polymyxin and NP200 based on Silico modeling method.

Intelectual Property IP
NOIGEL has patented pharmaceutical compositions as a nephroprotectors, which can reduce and eliminate Polymyxin nephrotoxicity.
• Based on polymyxin affinity to megalin, NOIGEL has defined **Nephroprotective agents - NP200**.
• NOIGEL researched thousands of FDA approved drugs and substances.
• Research led to discovery of nephroprotective agents (NP200)
  • NP200 has higher affinity for megalin than polymyxin.
  • NP200 has low or no overall toxicity to kidneys.
  • NP200 can be administered along with a polymyxin without compromising its antibacterial efficacy.
Finding the most suitable Nephroprotective agents:

- NOIGEL identified 246 substances from 21,000 FDA approved generic drugs.
- NOIGEL selected two substances best suitable as Nephroprotective agents (NP200).

Properties of NP200:

- NP200 is comprised of Quinones and Imidazole classes.
- NP200 has higher than Polymyxin affinity to kidney megalin receptor.
- NP200 has minimal spectrum of side effects to host body and doesn’t affect Polymyxin antimicrobial activity.
Experiment of 250 rats, ELISA-test and HPLC-systems were used. Studies were conducted during an 18 month period (in series).

2 groups (30 animals per group)

Results: 45 min after administration of NP200 (15 mg/kg) and colistin (0.5 mg/kg) intravenously (IV).
Study: kidney injury Polymyxin and NP200

- Neutrophil gelatinase-associated lipocalin (NGAL) - biomarker of acute kidney injury.
- N-acetyl-beta-D-glucosaminidase (NAG) - biomarkers of kidney disease (the 30 days after the last administration of polymyxin the excretion level of both compounds < 120 mkg /L )
Results: NP200 achieves goals

- Polymyxin kidney accumulation.
- Polymyxin nephrotoxicity biomarkers.

![Graph showing kidney concentration of Polymyxin (mk/kg tissue), (B).](image1)

Control (only Polymyxin) • NP200+ Polymyxin

![Graph showing excretion level, mk/kg/L.](image2)

Groups, n=30, p<0.05

Groups, n=15, p<0.05

- NGAL
- NAG
Key Takeaways

• No changes in the polymyxin chemical structure.

Prospects for Polymyxin clinical use:

Without NP200
1 week therapy with risk of nephrotoxicity.

With NP200
>1 week therapy without or mild nephrotoxicity.

The narrow range of action for infections that treatment can be stopped in 1 week.

The broader range of action for infections that require longer treatment.
Publications and IP for NP200

IP:

1. New combinatorial derivatives of antibiotics based on supramolecular structures PCT/RU2017/000424

2. Pharmaceutical composition for the treatment of infectious diseases based on polymyxin with nephroprotectors (Application filed 05/02/2018 with the PCT Patent Office)

Publications:


NexT STEPS

Nephroprotective agents NP200 with Polymyxin B can be leveraged in several ways:

• Pharmaceutical companies currently holding Polymyxin in their portfolio could use NOIGEL’S pharmaceutical composition to improve Polymyxin use efficiently and boost sales exponentially.

• Pharmaceutical companies currently holding generic Nephroprotective drugs NP200 in their portfolio could use them with additional new application, which will boost sales of NP200.

• Life Sciences private equity groups and venture capital firms could partner with NOIGEL.

• NOIGEL open for discussion of different types of collaboration as well.
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